

S/N 10/534894

PATENT**REMARKS**

Favorable consideration is respectfully requested in view of the above amendments and following remarks. The specification has been editorially amended to correct typographical, spelling, and grammatical errors as suggested by the Examiner. Claims 13-18, 25, and 26 are pending.

Turning to the substance of the Office Action, the specification has been objected to for informalities. Applicants respectfully submit that the specification has been amended to correct the typographical, spelling, and grammatical errors noted by the Examiner.

Withdrawal of the objection is respectfully requested.

Claims 13-18, 25, and 26 are rejected under 35 U.S.C. 101 for lack of utility. Applicants respectfully traverse the rejection to the extent it is maintained.

The rejection states that the claims are not supported by either a substantial or specific asserted utility or a well established utility. Applicants respectfully disagree with this position and contend that the claims are supported by specific utility.

Applicants submit that the specification sufficiently teaches at least that the polypeptide of SEQ ID NO: 2 and the polynucleotide of SEQ ID NO: 1 can be used to diagnosis the susceptibility of baldness or hairlessness in mice.

First, the claims relate to the amino acid sequence of SEQ ID NO: 2, which is a mice Rhor protein (identified as in the wildtype Balb/c mouse; see e.g. Example 1).

Second, on page 4 of the OA, the Examiner mentions that "*However, applicant has not identified any Rhor-related diseases (other than baldness) and has not provided evidence of a nexus between changes in expression or activity of Rhor protein and any human disease, or any type of human baldness. The disclosure teaches a gene, which applicants have identified as Rhor, wherein mutations of said gene is associated with baldness [paragraph 0021]. The Rhor mutation was identified in 'hairless' Balb/c mice; heterozygous mice exhibit sparse hair, while homozygotes are hairless [paragraph 0081]. DNA encoding the mutant protein comprises a 230 bp deletion in the genomic sequence of DNA encoding the wild-type protein [paragraph 0092].*"

S/N 10/534894

PATENT

Applicants, however, have identified baldness or hairless in mice as one kind of Rhor-related diseases for polypeptide of SEQ ID NO: 2 based on Examples 1-6 of Applicants' disclosure.

In particular, based on Examples 3 and 4, it is shown that a 230-bp deletion exists in both the genomic sequence and cDNA sequence. This 230-bp deletion is located in position 351-580 of SEQ ID NO: 1 and causes not only a 76aa deletion but also a frame-shift mutation which results in a 179aa mutated protein because a new stop codon is formed at position 538 of the mutated polynucleotide sequence (See enclosed Attachment A). Compared with the 827aa wildtype mice Rhor protein, it is predictable for the artisan that the majority of the activity of wildtype mice Rhor protein is lost.

Further, based on the structure analysis in Example 6, the mutated mice Rhor protein lacks the Rhomboid domain at amino acids 619-759 and the competence structure domain at amino acids 610-804 of SEQ ID NO: 2, suggesting the mutated mice Rhor protein does not have most (if not all) activity of wild type mice Rhor protein.

Since the baldness or hairless in mice is associated with mutation of mice Rhor polypeptide or the encoding sequence thereof, the invention as claimed is supported by a substantial and specific utility, in that the polypeptide of SEQ ID NO: 2 can be used to detect the susceptibility of baldness or hairless in mice. Moreover, although hairlessness is related to the mutated mice Rhor gene and protein, the wildtype mice Rhor gene and polypeptide are useful as negative controls during the detection. For example, they can be contained in the kit for detecting susceptibility of baldness or hairless in mice.

Summing up, based on the relationship between baldness in mice and the mutation of mice Rhor polypeptide of SEQ ID NO: 2, as disclosed and shown in the Applicants' disclosure, the claimed invention is supported by a specific utility, namely the diagnosis of the susceptibility of baldness or hairless in mice.

Favorable reconsideration and withdrawal of the rejection are respectfully requested.

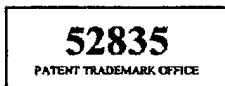
OCT 23 2008

S/N 10/534894

PATENT

Claims 13-18, 25, and 26 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. Applicants respectfully submit that this rejection should be withdrawn as the claims are supported by a specific utility which would enable one of skill in the art to use the claimed invention. Favorable reconsideration and withdrawal of the rejection are respectfully requested.

In view of the foregoing, Applicants believe that this application is in a condition for allowance. A Notice of Allowance is respectfully solicited. If any questions arise regarding this communication, the Examiner is invited to contact Applicants' representative at the number listed below.

Dated: October 23, 2008

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER &  
LARSON, P.C.  
P.O. Box 2902  
Minneapolis, MN 55402-0902  
(612) 455-3800

By: 

Bryan A. Wong  
Reg. No. 50,836  
BAW/ev

\* Attachment A

the amino acid sequence of mutated mice Rhor protein (length=179aa)

```

atg gcc tca gct gac aag aat ggc agc aac ctc cca tct gtg tct ggt      48
Met Ala Ser Ala Asp Lys Asn Gly Ser Asn Leu Pro Ser Val Ser Gly
1         5         10        15
agc cgc ctg cag agc cgg aag cca ccc aac ctc tcc atc acc atc ccg      96
Ser Arg Leu Gln Ser Arg Lys Pro Pro Asn Leu Ser Ile Thr Ile Pro
20        25        30
cca cca gag agc cag gcc ccc ggc gag cag gat agc atg ctt cct gag      144
Pro Pro Glu Ser Gln Ala Pro Gly Glu Gln Asp Ser Met Leu Pro Glu
35        40        45
agg cgc aag aac cca gcc tac ctg aag agt gtc agc cta cag gag ccc      192
Arg Arg Lys Asn Pro Ala Tyr Leu Lys Ser Val Ser Leu Gln Glu Pro
50        55        60
cgg gga cga tgg cag gag ggc gca gag aag cgc ccc ggc ttc cgc cgc      240
Arg Gly Arg Trp Gln Glu Gly Ala Glu Lys Arg Pro Gly Phe Arg Arg
65        70        75        80
cag gcc tcc ctg tcc cag agc atc cgc aag agc aca gcc cag tgg ttt      288
Gln Ala Ser Leu Ser Gln Ser Ile Arg Lys Ser Thr Ala Gln Trp Phe
85        90        95
ggg gtc agc ggc gac tgg gag ggc aag cga caa aac tgg cat cgt cgc      336
Gly Val Ser Gly Asp Trp Glu Gly Lys Arg Gln Asn Trp His Arg Arg
100       105       110
agc ctg cac cac tgg tgt ccg ctc tgg cta ctc cca tct gcc ccg ccg      384
Ser Leu His His Trp Cys Pro Leu Trp Leu Leu Pro Ser Ala Pro Pro
115       120       125
caa gag gat atc tgt tgc cca tat gag ctt tca ggc agc cgc cgc cct      432
Gln Glu Asp Ile Cys Cys Pro Tyr Glu Leu Ser Gly Ser Arg Arg Pro
130       135       140
cct caa ggg gcg ttc cgt gct aga tgc gac tgg gca gcg gtg ccg gca      480
Pro Gln Gly Ala Phe Arg Ala Arg Cys Asp Trp Ala Ala Val Pro Ala
145       150       155       160
tgt caa acg cag ctt cgc tta ccc cag ctt cct gga gga gga tgc tgt      528
Cys Gln Thr Gln Leu Arg Leu Pro Gln Leu Pro Gly Gly Gly Cys Cys
165       170       175
cga tgg agc tga caccttc gactcctcct ttttagtaa ggaagaaatg      577
Arg Trp Ser *

```

## Note:

(a) The underlined portion is different from the wildtype mice Rhor protein as shown in SEQ ID NO: 1 or 2 .

(b) \* means a stop codon.